

Claims

- [001] A mammalian cell comprising
- a. a responsive transcription factor RTF, which modulates transcription of OP operator-containing promoters in response to compounds being gaseous or liquid at the cultivation temperature of said mammalian cell;
 - b. a promoter or promoter fragments operatively linked to OP operator sites specific for binding of said RTF.
- [002] The mammalian cell of claim 1 further comprising a nucleic acid encoding a desired protein functionally linked to said promoter or promoter fragments operatively linked to OP operator sites specific for binding an RTF.
- [003] The mammalian cell of claim 1 or 2, wherein binding of the RTF to OP-containing promoters is changed in response to compounds being gaseous at the cultivation temperature of said mammalian cell.
- [004] The mammalian cell of claim 1 or 2, wherein binding of the RTF to OP-containing promoters is changed in response to compounds being liquid at the cultivation temperature of said mammalian cell.
- [005] The mammalian cell of claim 1, wherein the RTF comprises amino acid sequences related to or derived from naturally occurring proteins.
- [006] The mammalian cell of claim 1 or 2, wherein the RTF comprises amino acid sequences related to or derived from non-mammalian proteins.
- [007] The mammalian cell of claim 1 or 2, wherein the RTF is the *Aspergillus nidulans* AlcR protein.
- [008] The mammalian cell of claim 1 or 2, wherein the RTF is the *Pseudomonas putida* AlkS protein.
- [009] A non-human mammal comprising at least one mammalian cell as claimed in claim 1 or 2.
- [010] A method for adjusting the expression level of a desired protein in a mammalian cell as claimed in claim 2, comprising culturing said mammalian cell and modulating gene expression by administration of a compound for which transcription of the OP operator-containing promoter and the responsive transcription factor RTF are responsive.
- [011] The method of claim 10, wherein the protein is selected from the group consisting of SEAP, a fluorescent protein, human growth hormone, alpha-interferon, beta-interferon, gamma-interferon, insulin, erythropoietin, tissue plasminogen activator, DNase, a monoclonal antibody, Factor VIII, Factor VII, HAS, IL-2, glucagons, EGF, GCSF, GMCSF, thrombopoietin, gp160, HbSAg, a protein encoded by a tumor suppressor gene, and a protein encoded by a gene in-

- terfering with absorption, distribution, metabolism and excretion of compounds contained in tobacco smoke.
- [012] The method of claim 10, wherein the compound for modulating gene expression is selected from the group consisting of ketones, aldehydes, haloalkanes, alcohols, esters, amines, and ethers.
- [013] The method of claim 10, wherein the compound for modulating gene expression is selected from the group consisting of ethanol, methylamine, ethylamine, n-propylamine, n-butylamine, n-pentylamine, n-hexylamine, benzylamine, 2-butanone, ethanol, n-propanol, n-butanol, 2-propanol, 2-butanol, 2-methylbutyraldehyde, acetaldehyde, propanal, acetone, 2-butanone, 2-pentanone, 3-pentanone, cyclohexanone, glycoaldehyde, glyoxal, glyoxylate, ethylene glycol, ethanolamine, ethyl acetate, ethyl ether, and dicyclopropylketone, and compounds that are metabolized *in situ* to said members of the group.
- [014] The method of claim 10, wherein the compound for modulating gene expression is selected from the group consisting of ethanol, methylamine, ethylamine, n-propylamine, n-butylamine, n-pentylamine, n-hexylamine, benzylamine, 2-butanone, ethanol, n-propanol, n-butanol, 2-propanol, 2-butanol, 2-methylbutyraldehyde, acetaldehyde, propanal, acetone, 2-butanone, 2-pentanone, 3-pentanone, cyclohexanone, glycoaldehyde, glyoxal, glyoxylate, ethylene glycol, ethanolamine, ethyl acetate, ethyl ether, and dicyclopropylketone.
- [015] The method of claim 10, wherein the RTF comprises amino acid sequences related to or derived from non-mammalian proteins.
- [016] The method of claim 10 wherein the RTF is the *Aspergillus nidulans* AlcR protein and the compound for modulating gene expression is acetaldehyde.
- [017] A method for adjusting the expression level of a gene in a mammalian cell as claimed in claim 1, comprising
- a. functionally linking said gene to an OP-containing promoter,
 - b. transferring said OP-containing promoter functionally linked to said gene into said mammalian cell, and
 - c. inducing expression of said gene by activating said OP-containing promoter by administration of a compound for which the OP operator-specific responsive transcription factor RTF is responsive.
- [018] The method of claim 17, wherein the gene codes for a protein selected from the group consisting of SEAP, a fluorescent protein, human growth hormone, alpha-interferon, beta-interferon, gamma-interferon, insulin, erythropoietin, tissue plasminogen activator, DNase, a monoclonal antibody, Factor VIII, Factor VII,

- HAS, IL-2, glucagons, EGF, GCSF, GMCSF, thrombopoietin, gp160, and HbSAg.
- [019] The method of claim 17, wherein the gene is a tumor suppressor gene.
- [020] The method of claim 17, wherein the gene is a gene interfering with absorption, distribution, metabolism and excretion of compounds contained in tobacco smoke.
- [021] The method of claim 17, wherein the compound for which the OP operator-specific responsive transcription factor RTF is responsive is selected from the group consisting of ketones, aldehydes, haloalkanes, alcohols, esters, amines, and ethers.
- [022] The method of claim 17 wherein the compound for which the OP operator-specific responsive transcription factor RTF is responsive is selected from the group consisting of ethanol, methylamine, ethylamine, n-propylamine, n-butylamine, n-pentylamine, n-hexylamine, benzylamine, 2-butanone, ethanol, n-propanol, n-butanol, 2-propanol, 2-butanol, 2-methylbutyraldehyde, acetaldehyde, propanal, acetone, 2-butanone, 2-pentanone, 3-pentanone, cyclohexanone, glycoaldehyde, glyoxal, glyoxylate, ethylene glycol, ethanolamine, ethyl acetate, ethyl ether, and dicyclopropylketone, and compounds that are metabolized *in situ* to said members of the group.
- [023] The method of claim 17 wherein the compound for which the OP operator-specific responsive transcription factor RTF is responsive is selected from the group consisting of ethanol, methylamine, ethylamine, n-propylamine, n-butylamine, n-pentylamine, n-hexylamine, benzylamine, 2-butanone, ethanol, n-propanol, n-butanol, 2-propanol, 2-butanol, 2-methylbutyraldehyde, acetaldehyde, propanal, acetone, 2-butanone, 2-pentanone, 3-pentanone, cyclohexanone, glycoaldehyde, glyoxal, glyoxylate, ethylene glycol, ethanolamine, ethyl acetate, ethyl ether, and dicyclopropylketone.
- [024] The method of claim 17 wherein the OP-containing promoter is an AlcR-specific OP site, RTF is the *Aspergillus nidulans* AlcR protein, and the compound for which RTF is responsive is acetaldehyde.
- [025] An isolated nucleic acid useful for constructing a mammalian cell as claimed in claim 1, comprising an RTF-encoding nucleic acid functionally linked to a promoter useful for expression of the RTF in said mammalian cell.
- [026] The isolated nucleic acid of claim 25 comprising an OP sequence functionally linked to a promoter or a fragment thereof useful for RTF-dependent gene expression in said mammalian cell.
- [027] The isolated nucleic acid of claim 25 or 26 further comprising genetic elements useful for construction of viral vectors.